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Committee to Advise on Tropical Medicine and Travel (CATMAT)

STATEMENT ON MENINGOCOCCAL VACCINATION FOR TRAVELLERS

Meningococcal infection is severe, with a case-fatality rate of 15% or more. The disease occurs sporadically worldwide and in focal epidemics. Spread of the organism is by the respiratory route. Certain areas of the world have predictable periods of meningococcal disease activity, which may pose a risk to international travellers or Canadians working abroad.

Exposure risk even within the known geographic areas of meningococcal disease activity may be very difficult to predict because transmission occurs at variable rates. Thus, place and duration of exposure are not the only factors to consider. Climatic conditions, which vary from year to year, have a major impact on the intensity of risk. Nature of exposure, such as crowded, intimate or institutional living within a disease activity area is also important. In addition, the current health of the traveller must be considered. Age is a major determinant of disease risks. Among recent cases in Canada, 29.1% occurred in infants < 2 years of age, 42.4% in children aged 2 to 19 years, and 28.6% in persons > 19 years of age (LCDC, unpublished data). Similar data have been reported from the United States[1]. Splenectomy and immune function are also important risk determining features.

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STATEMENT 1

Epidemic Pattern of Meningococcal Disease in Developing Nations

The epidemic pattern in developing nations where meningococcal disease is active indicates that children are at the greatest risk of disease, and that the peak incidence may occur in those < 2 years of age. In addition, data indicate that there is an appreciable risk of disease in adulthood.

Recommendation

Category A (Good evidence to support statement) (For an explanation of evidence-based medicine, please see CCDR 1994;20:145-47[2].)

Grade III (Evidence from descriptive studies)

The traditional **endemic** meningococcal meningitis areas of the world include regions of sub-Saharan Africa [see Map 1 and the list of countries at the end of this statement (WHO unpublished data)]. Disease occurrence in these areas is seasonal and can greatly exceed that found in other parts of the world.

In addition to areas with predictable meningococcal activity, areas of new activity are identified in frequent updates published by the Laboratory Centre for Disease Control, Health Canada, and should be used to assess the need for vaccination. Prior to making the decision to recommend vaccination against meningococcal disease, considerable clinical judgement needs to be exercised in the assessment of the international traveller, taking into account potential geographic exposure, personal health, and planned activities.

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The meningococcal polysaccharide vaccines licensed in Canada are safe, immunogenic, and include the serogroups A and C, which are most commonly associated with epidemics of the disease. They should be considered for "at-risk" individuals who are in, or who will be in, a zone of increased meningococcal disease caused by one of the serogroups represented in the vaccine.

STATEMENT 2
Age-Specific Immune Response to Meningococcal Vaccines

Age-specific immunogenicity against group A meningococcal polysaccharide in children aged 3 to 5 months is poor 3 months after receiving two doses of monovalent vaccine: serum antibody to group A meningococcal polysaccharide is < 2 µg/mL (36%) and 1 µg/mL (60%)[3,4]. Similarly, children immunized at 3, 7 and 12 months of age with either A and/or C vaccine demonstrated rapidly declining antibodies between 13 and 24 months of age. A more dramatic decline in group C antibodies was observed[4,5].

In a more recent report following the vaccination program in Ottawa, antibodies were measured in 50 children aged 6 to 12 months. At one month following immunization, a very modest antibody response was seen to group A: 0.13 µg/mL (pre) to 1.58 µg/mL (post). In addition, the researchers reported a poor correlation in bactericidal activity and antibody levels to group C in very young children[5,6].

Recommendation

Category A (Good evidence to support statement)

Grade II (Evidence from cohort studies)

STATEMENT 3
Vaccine Efficacy

Vaccine efficacy against group A meningococcal disease declines rapidly in children immunized with a single dose of vaccine at < 4 years of age (vaccine efficacy at 1, 2, and 3 years post-vaccination is 100%, 52%, and 8%, respectively). Similar poor responses to polysaccharide A have been shown with quadrivalent- combined vaccine in children aged 2 to 8 years at one year follow-up[4,6,7].

Recommendation

Category A (Good evidence to support statement)

Grade II (Evidence from case-control study)

STATEMENT 4
Timing of Primary Immunization, and Need for Booster Doses of Meningococcal Vaccine

Giving a booster dose of vaccine against group A and C meningococcal disease following primary immunization (with one or two doses of either A or C vaccine) has been studied for bivalent vaccine A + C given to healthy North American children at ages 2 years and 5.5 years[4,8].

Recommendation

Category A (Good evidence to support statement)

Grade II (Evidence from cohort study)

Primary immunization of African children between the ages of 1 to 4 years with a single dose of bivalent vaccine A + C showed a decline of antibody to group A at 2 years and 5 years after vaccination. This decline in antibody was not influenced by a booster dose of vaccine given 2 years after immunization[2,8].

Recommendation

Category A (Good evidence to support statement)

Grade II (Evidence from cohort study)

The primary vaccination schedule should follow the recommendations contained in the ***Canadian Immunization Guide***, 4th edition, published by Health Canada. Protective immunity is established about 15 days after vaccination and is estimated to last for at least 3 to 5 years in adults.

The following individuals should be considered for immunization when visiting countries with an increased risk of meningococcal infection.

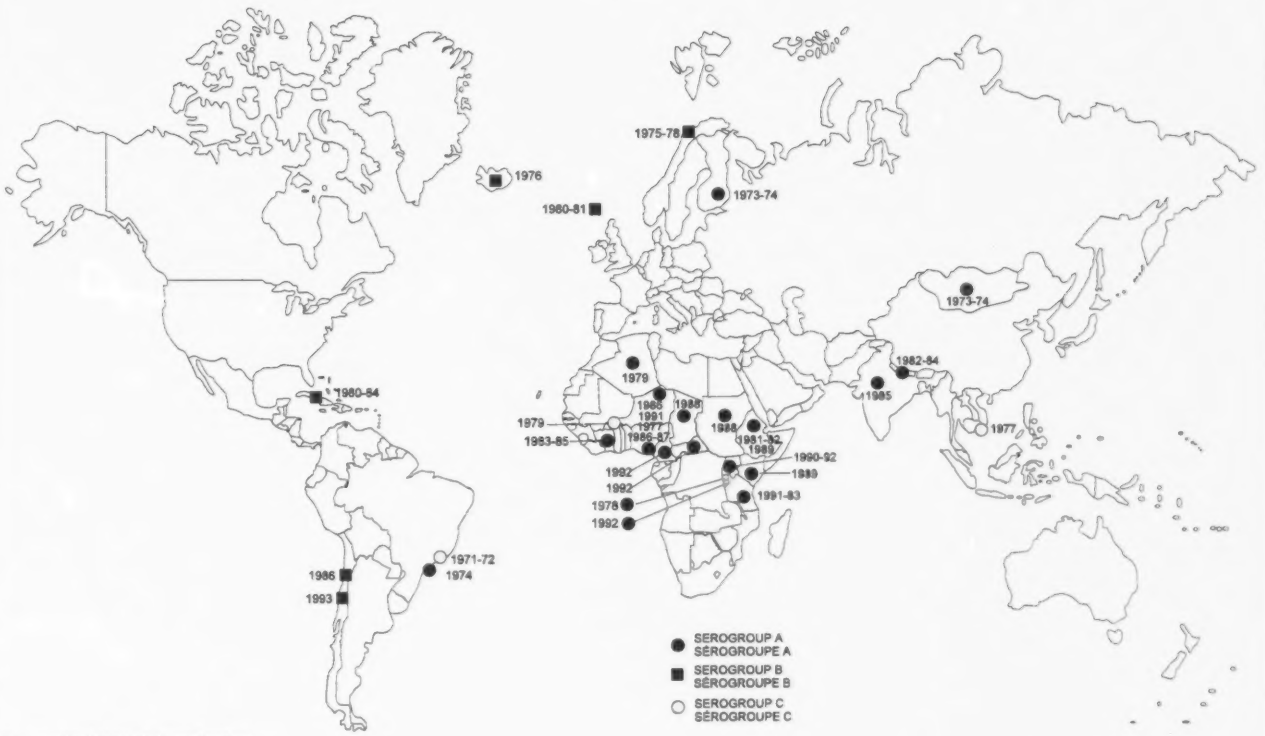
1. Adolescents and children who are in, or will be travelling to, an area of **epidemic** meningococcal activity. Serogroup A vaccine may be less than fully effective in children 6 to 11 months of age. Serogroup C vaccine has not been shown to be effective in children < 2 years of age.
2. Individuals working in hospitals, health care, field epidemiology, research, international aid or refugee camps in areas of meningococcal **epidemic** activity.
3. Individuals who will be working or living in the "traditional" **endemic** meningococcal areas of the world, i.e., sub-Saharan Africa.
4. Individuals who will be involved in activities that the local health authority or government would consider at risk for acquiring meningococcal disease.
5. Individuals such as flight attendants and cabin crews, military or intelligence personnel who travel extensively and unpredictably.
6. Individuals making contact with traditional life in rural parts of endemic areas.
7. Pilgrims to Mecca for the annual Haj or Umra. Saudi Arabia requires evidence of vaccination against meningococcal meningitis for these individuals.

Vaccination is NOT recommended for short-term travellers on business or holiday to areas of heightened meningococcal activity who will have little contact or exposure to local populations in crowded conditions.

The following countries have frequent epidemics of meningococcal meningitis, mostly serotype A and especially during the dry season (December through June). These countries are in what is known as the sub-Saharan African meningococcal meningitis belt.

Benin	Guinea Bissau
Burkina Faso	Mali
Cameroun	Niger
Central African Republic	Nigeria
Côte d'Ivoire	Rwanda
Djibouti	Senegal
Ethiopia	Somalia
Gambia	Sudan
Ghana	Tchad

Map 1
Major epidemics of meningococcal meningitis from 1970–1993



Source: World Health Organization

Guinea
Togo

In the recent past, the following countries reported epidemic or significant outbreaks of meningococcal meningitis.

Brazil (serotype B)
Burundi
Chile
Cuba
Haiti
India
Kenya
Malawi
Nepal
Tanzania
Uganda

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ISONIAZID CHEMOPROPHYLAXIS FOR DUAL HIV-TB INFECTION: A CAUTIONARY TALE

Introduction

Infection with human immunodeficiency virus infection (HIV) is the single most important risk factor for the progression of dormant tuberculous infection to active tuberculous disease[1]. In contrast to the lifetime 10% risk for a non-HIV-infected immune competent subject, in the presence of dual HIV-TB infections there is an 8% to 10%[2] annual and ongoing risk for the development of active TB. For this reason, it is strongly recommended that subjects who are HIV infected should be screened for the presence of tuberculous infection and, if found, isoniazid (INH) chemoprophylaxis be offered[3]. The use of INH in this situation not only reduces the risk of subsequently developing TB but at least initially appears to slow the progression of HIV infection to AIDS and death[4].

The following case report highlights the need for careful evaluation of such subjects and the potentially disastrous consequences of failure to do so.

A 41-year-old male, recently diagnosed as being HIV positive, was referred for evaluation for possible INH chemoprophylaxis. His risk factor for HIV infection was sex with men and he denied any history of intravenous drug use. He had a chronic "smoker's" cough but had noticed no recent change. There was no history of weight loss, and minimal sputum was produced. He had a remote history of working on a Native Indian Reserve in the past but had no known contact with TB at that time. His purified protein derivative (PPD) skin test had been recently carried out and he was found to have a 40 mm positive response. His CD4 count was 400.

There had been no prior history of opportunistic infections. As a baseline evaluation and because of the importance of ruling out active TB, he had a chest x-ray, which was reported as normal, and sputum was obtained for acid-fast bacilli (AFB) smear and culture. The sputum was negative on smear and the subject was counselled to discuss the option of chemoprophylaxis with his family doctor and return in 6 weeks for a final decision regarding initiating chemoprophylaxis. Four weeks after the initial evaluation, the sputum sample was reported as growing Mycobacterium tuberculosis and the patient was recalled. His symptoms remained unchanged and the only event of note was that the subject had attended a community AIDS resource centre the previous week for counselling. At that time, a one-on-one interview was held. With the confirmed positive M. tuberculosis culture, anti-tuberculous drugs were initiated.

Discussion

This case report highlights the importance of considering TB infection in HIV-infected subjects and, prior to initiating chemoprophylaxis, ruling out current active disease[3,4]. Failure to rule out active disease at baseline could have led to the initiation of INH and possible development of INH resistance due to the use of mono-drug therapy for active disease. In addition, transmission of TB to HIV-infected contacts or community workers is a concern, with the added risk in a significant percentage for the development of active disease.

The presence of TB infection is usually evaluated by skin testing with 5 tuberculin units (TU) PPD. Five mm or more of induration is diagnostic of tuberculous infection in the presence of HIV infection or where contacts of an active case are being evaluated[5]. A negative response may be a true negative or, in the presence of anergy, may be a false negative response. Interpretation of a negative response in the presence of anergy is difficult and in some instances, especially if the subject is from a population with a high prevalence of TB infection (in a Canadian context — Aboriginal Canadians or immigrants from Type II countries, e.g., sub-Saharan Africa[6]), empiric INH chemoprophylaxis has been suggested. Before intervention is begun, the clinician must rule out current active disease, as is exemplified by this case report.

A minority of persons with TB may have a normal chest x-ray. This is especially true in HIV-associated TB[7]. Consequently, at all times, sputum for AFB should be obtained. Four to 6 weeks are usually required for culture results to be available and during this time the subject can discuss the risk/benefit ratio with his family physician. If the chest x-ray is abnormal and the smear is negative, earlier more aggressive evaluation, possibly including sputum induction and/or bronchoscopy, is indicated.

The need to include TB in the differential diagnosis of all subjects with HIV is important. Although the prevalence of HIV-related TB is low in Canada[8], there are potentially disastrous consequences when an undiagnosed case of active TB disease is a member of the HIV-infected community. The delay in diagnosis of active TB has been shown to cause significant clustering of TB cases in HIV[9] and non-HIV settings[10].

Community agencies should be aware of the signs and symptoms of TB: classic cough, sputum production, night sweats and fever[11] but, in some instances, they may be more subtle and careful collection of body secretions, primarily sputum for AFB smear and culture, is strongly recommended.

Appropriate education of clients, community-based organization workers, as well as health care workers is important. Rigorous use of masks, ultraviolet light and negative pressure ventilation has been recommended by U.S. authorities[12], but we suggest a more balanced approach based on the level of risk exposure[13]. In most communities offering services to HIV-infected persons, risk of exposure to an active case of TB is low. However, community-based organizations offering services to populations known to be at greater risk for TB should exercise greater caution and have a high index of suspicion for the disease. Populations with a higher risk for TB in Canada include First Nations, persons and their families immigrating to Canada from countries reporting high rates of TB, street involved, homeless or those with unstable housing, and injection drug users. Although targeting of high-risk groups has been considered important, recent molecular epidemiology studies of TB transmission has demonstrated significant risk of disease being spread to non high-risk groups[14]. The current Canadian AIDS Society initiative in TB should sensitize the at-risk communities to the dangers of dual HIV/TB infection and focus our attention on disease prevention by INH chemoprophylaxis and early consideration of the possibility of TB as a diagnosis. Prompt initiation of TB therapy is the most effective intervention to reduce the risk of transmission of TB infection to family, friends, treatment and support workers and to community members, irrespective of HIV status.

Acknowledgements

I would like to acknowledge helpful comments from Drs. Maura Ricketts and Don Sutherland.

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Source: *JM FitzGerald, MB, Willow Chest Centre, Division of TB Control, B.C. Centre for Disease Control, Vancouver, British Columbia.*

Editorial Comment: Approximately 2,000 cases of active TB are diagnosed and reported each year in Canada. The incidence rate of TB in Canada is among the lowest in the world (7.4 per 100,000) and remains stably low after decades of decline. Over half of all TB cases in Canada are diagnosed among foreign-born Canadians. Almost 40% of the Canadian-born TB cases are among First Nations people.

In 1984 in the United States, the rate of new TB cases began to increase. This increase has been attributed directly to the failure to fund TB control programs adequately, to patterns of immigration from TB-endemic countries, and to the interaction of TB and HIV in under-serviced populations. Unlike the U.S., Canada has not yet seen an increase in TB cases. However, the decline in TB rates in Canada ended in 1987-88, approximately 3 years after the downward trend in the incidence of TB ended in the U.S. At this time, in Canada, there is no evidence that the arrest in decline of the TB incidence rates is due to TB/HIV interactions. It appears that patterns of immigration into Canada from TB-endemic countries and clusters of TB in First Nations populations, alcohol abusers and injection drug users are responsible for the majority of cases.

In Canada, we face several important challenges to public health including the following: continued immigration of TB infected (inactive) people; establishing national goals; targeting stubborn high prevalence or incidence pockets; prevention of the pattern of increased TB and TB/HIV coinfection as seen in the U.S.; prevention of the emergence of multidrug-resistant TB (MDR-TB); and preparation of the health care communities (both HIV and TB) to cope with possible TB/HIV interaction. To do this, we must reduce the transmission of TB, prevent reactivation of old TB, and ensure appropriate and complete therapy. Programs designed to achieve these goals must be made available to all Canadians, with the focus on high-risk populations but, arguably, must also be targeted at the HIV-affected community.

Some important initiatives have already begun. For example, in 1992, LCDC published Guidelines for the identification, investigation and treatment of individuals with concomitant tuberculosis and human immunodeficiency virus infection, and in 1993, organized a conference on TB/HIV coinfection in Toronto. LCDC has recently conducted a consensus meeting to review it's role in the management of TB. In addition, Canadian guidelines for the prevention of TB transmission in health care facilities are currently being prepared for publication. The Canadian AIDS Society has developed and conducted an important workshop to inform and educate community-based care, treatment and support workers about TB/HIV coinfection. The workshop provides education about the medical and environmental prevention of TB transmission, as well as addresses the human rights issues around TB/HIV coinfection.

This case report demonstrates that preventing an outbreak of TB in an HIV setting will require partnership and commitment from many individuals, including clinicians, staff and volunteers of community-based service organizations, housing and care providers, hospitals, hospices, palliative care units, governments at all levels, and clients. A high index of suspicion plus the necessary TB services infrastructure and a well-informed clientele are key to TB control. However, TB in the context of HIV infection will also require commitment by providers to obtain informed consent, and to provide pre-test and post-test counselling and non-coercive treatment modalities. Public health departments can expect requests for consultation on TB control in HIV-infected or HIV at-risk populations. The development, resourcing and implementation of effective programs should not be constrained by limited resources or by the low levels of TB/HIV coinfection in Canada. On the contrary, the investment in preventing TB infection

(primary prevention) and preventing TB disease (secondary prevention) must be viewed as an investment to prevent larger expenditures on tertiary interventions, outbreak management and MDR-TB. A single case of MDR-TB may incur health care expenditures in excess of $250,000. Finally, there is the human toll: MDR-TB has a high death rate.

TB/HIV coinfection will bring many human rights issues to the forefront, particularly those surrounding mandatory therapy and daily observed prophylaxis/therapy. For HIV-infected individuals, confidentiality and privacy are vital because of the potential harm to them if their HIV status becomes known beyond the circle of those in whom they have chosen to confide. TB control programs will be challenged by these principles in order to fulfil their mandates. HIV/AIDS programs will face challenges in trying to prevent and treat a disease that is casually communicable and for which an established control program already exists.

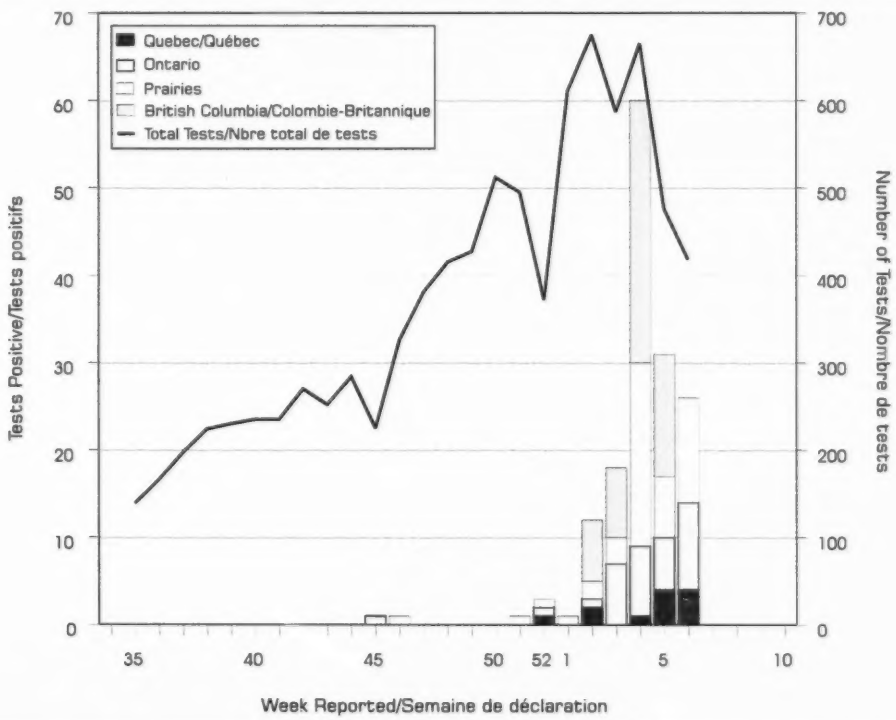
RESPIRATORY DISEASE SURVEILLANCE
(as of 10 February, 1995)

Influenza

The Laboratory Centre for Disease Control has received reports of 154 influenza virus detections since September 1994. The distribution of reports over time and by region is presented in Figure 1. Most (118; 77%) of the reports were of influenza A virus detections; the remaining 36 (23%) were of influenza B. Reports by provincial epidemiologists on the extent of influenza activity in the community indicated that sporadic cases of influenza-like illness were recorded in late October and November in four provinces (Newfoundland, Ontario, Alberta, and British Columbia) and in Saskatchewan in January. Localized outbreaks were reported from Newfoundland from mid-December, and British Columbia and Saskatchewan in January. To date, no province or territory has recorded widespread activity of influenza-like illness this season.

Influenza activity has been moderate in North America and Europe so far this season. However, the World Health Organization (WHO) reports that influenza A(H3N2) and influenza B are spreading on both continents. In late January, 11 U.S. states reported regional and widespread activity, and influenza virus

Figure 1
Positive Influenza Tests in Canada by Region and Week of Report



detections have been reported from 41 states and the District of Columbia. Influenza A (H3N2) predominates in all regions except the South Atlantic and mountain regions.

Apart from an outbreak of influenza B in Portugal early in the season, only sporadic cases of both influenza A and influenza B have been reported from most European countries. However, there were outbreaks of influenza A in Spain in the second half of January, and Madrid reported epidemic levels of activity at the end of the month.

Source: *Laboratories contributing to the Respiratory Virus Surveillance Program, Disease Surveillance Division, Bureau of Communicable Disease Epidemiology, LCDC, Ottawa, and WHO.*

Notifiable Diseases Summary

We have excluded this table from the FAX issue of Canada Communicable Disease Report for those readers who do not need this information. For those readers interested in this table, call the FAX line and select the index to get the access number.

Notifiable Diseases Summaries published to date in this new format (FAX) can be found in the index under the same name.

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